Dimebon enhances hippocampus-dependent learning in both appetitive and inhibitory memory tasks in mice

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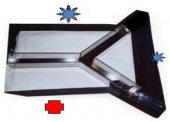
INTRODUCTION

We aimed to investigate the procognitive effects of dimebon, and study whether repeated or acute intraperitoneal injection of this compound, at doses known to increase memory, affect learning scores in appetitive (Y-Maze) and inhibitory (step-down avoidance) tasks in two strains of mice (CD1 and C57BL/6N). Additionnal behavioural tests (O-maze, novel cage and water consumption tests) were carried out to address possible non-specific effects of dimebon on parameters of drinking, anxiety and exploration/locomotion.

Y-maze apparitus



Step down avoidance

RESULTS

1. Subchronic treatment with dimebon accelerates learning and increases duration of drinking behaviour in an appetitive memory task in C57BL/6N mice while thirst and behaviours in other tests were not affected.

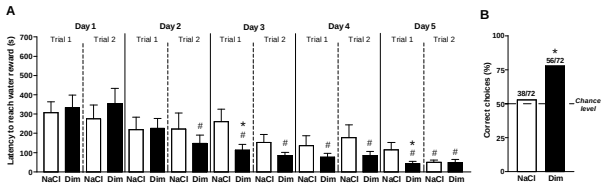


Figure 1 : Effects of daily administration of dimebon (0.1 mg/kg) on learning in the Y-Maze in C57BL/6N mice. *Dimebon-treated group showed significant decrease latencies to reach the water reward on days 2-5 of training, while vehicle-treated group demonstrated this reduction only on day 5 (# p<0.05) (A). This parameter was significantly shorter in dimebon- than in vehicle-treated mice on days 3 and 5 (*p<0.05). The percentage of correct choices for the arm with the filled bottle was significantly higher in dimebon-treated group than in control group (*p<0.05) (B). Dim: dimebon; NaCl: vehicle.*

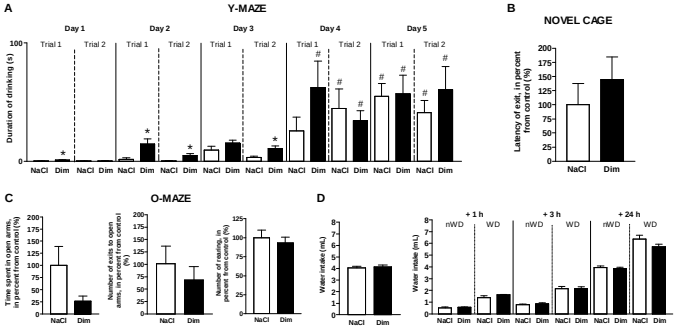


Figure 2 : Effects of repeated treatment with dimebon on parameters of anxiety, locomotion, exploration and drinking in mice. *Mice treated with dimebon or vehicle both showed a significant progressive increase of drinking behaviour in the Y-Maze (# p<0.05). Duration of drinking was significantly higher in dimebon-treated group than in control group (*p<0.05) (A). Mice repeated administered with dimebon did not differ from vehicle-treated animals in the O-maze (B), the novel cage (C), 24-h water intake (D) tests. Acute treatment with dimebon did not affect 1-, 3-, and 24-h intake (E). WD: water-deprived, nWD: non-water-deprived.*

2. Bolus treatment with dimebon increases the performance in an inhibitory memory task in C57BL/6N but not in CD1 mouse strain.

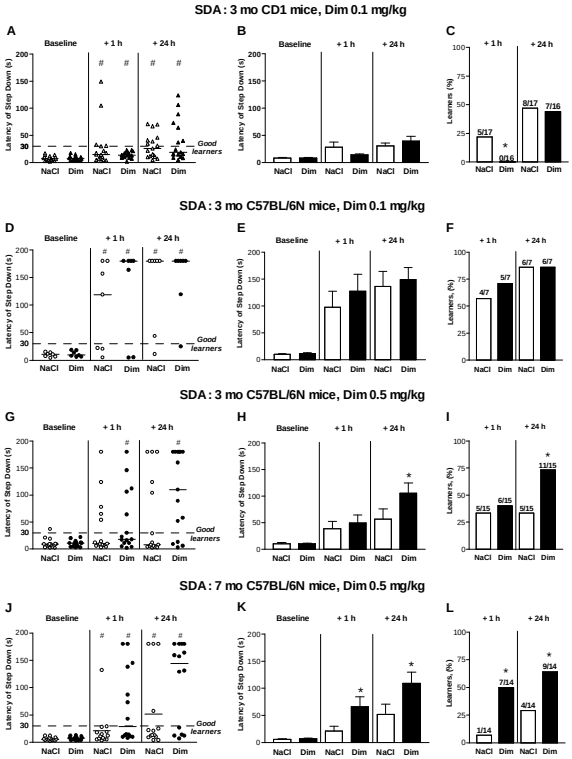


Figure 3 : Effects of bolus treatment with dimebon on 3-month-old (3 mo) CD1 mice and on 3- and 7-month-old (7 mo) C57BL/6N mice in the step-down avoidance. *CD1 and C57BL/6N mice showed an increase in scores of learning in both recall sessions (+1h, +24h) in comparison to the training session (baseline) (A),(D),(G),(J). 3 and 7 mo C57BL/6N mice treated with dimebon at the dose of 0.5 mg/kg showed significantly increased latencies of step down, as well as significantly higher percentage of good learners, 24h after training in comparison to the vehicle-treated group (H),(I),(K),(L). A lower dose of dimebon (0.1 mg/kg) did not affect the scores of learning in neither C57BL/6N or CD1 mice (B,C,E) exception of the percentage of good learners that was surprisingly reduced in dimebon-treated group in the first recall session for CD1 strain (B).*

CONCLUSION

- Administration of dimebon via repeated (0.1 mg/kg) and acute (0.5 mg/kg) i.p. injections respectively increases learning scores in Y-Maze and step-down avoidnace tasks in C57BL/6N mice.
- Acute treatment with dimebon at the dose 0.1 mg/kg did not affect learning scores in either 3-month-old C57BL/6N or CD1 mice and dimebon seems to have an opposite effect in CD1 strain
- No effects of 3-day administration with dimebon were observed on the parameters of thirst, anxiety, and exploration/locomotion
- In conclusion: dimebon enhances hippocampus learning in both appetitive and inhibitory tasks in C57BL mice